PHARMACOLOGY, MEDICAL REPORTS, ORTHOPEDIC, AND ILLNESS DETAILS (COMORBID) Volume 1 ISSUE 1 (2022)

HEADACHE PROFILE AND ASSOCIATED SYMPTOMS IN INTRACRANIAL TUMORS

Adhitya Riski Apriady¹, Yusuf Wibisono², Asep Nugraha Hermawan³

Medical Education Study Program, Faculty of Medicine, Padjadjaran University, Bandung, West Java, Indonesia

^{2,3} Department of Neurology, Faculty of Medicine, Padjadjaran University, Bandung, West Java, Indonesia

E-mail: 1) adhityariski@gmail.com

Abstract

Intracranial tumors are rare in headache sufferers, although headache is common in intracranial tumor patients. This limits the utility of headache symptoms to make a diagnosis, and it's crucial to know whether people with intracranial tumors have specific headache criteria. Other investigations do not support the classic criteria for headache in intracranial tumors, such as progressive, worse in the morning, and exacerbated by Valsalva maneuvers. Clinical studies found that headache as the sole symptom was rare, and only occurred in 2% of patients, hence this study also investigated the prevalence of nausea/vomiting, seizures, loss of consciousness, and motor deficits. This study uses resumes of medical records of patients diagnosed with intracranial tumors and hospitalized in the Department of Neurology, dr. Hasan Sadikin Central General Hospital West Java, Indonesia. While the sampling method in this study was total sampling, by taking all medical record resumes of patients with intracranial tumors from January to December 2018. Headache was a prevalent symptom of intracranial tumors in this study, occurring in 75,3 % of the subjects and was usually accompanied by other symptoms, especially motor deficits (64,5%), loss of consciousness (60,2%), nausea and vomiting (31) 2%), and seizures (23,7%). Patients were most likely to have bilateral headaches (62,5%), and 63,6% of patients who had unilateral headaches had a unilateral intracranial tumor on the same side of the headache. Patients who experienced progressive headaches were 93,5% of patients. While, the most common headache onset in patients with intracranial tumors before hospital admission were; 3-30 days (40,4%) and > 30 days - 6 months (38,5%).

Keywords: Decreased Consciousness, Motor Deficit, Nausea, Vomiting, Seizures

1. INTRODUCTION

Patients with intracranial tumors are more likely to experience headaches, with prevalence rates ranging from 32.2% to 71% (Nelson & Taylor, 2014). While, the estimated global prevalence of headache in adults (symptomatic at least once in the past year) is around 50% (WHO, 2018). The significance of headache symptoms in making a diagnosis is therefore limited, and it is vital to determine if patients with intracranial tumors have unique criteria for headaches (Taylor, 2014).

Furthermore, the classic criteria for headache in intracranial tumors mentioned in *International Classification of Headache Disorders-3* (ICHD-III) describes headaches that are usually progressive, worse in the morning, and exacerbated by Valsalva-like maneuvers, caused by one or more intracranial tumors (Arnold, 2018). The literature review by Nelson

S. and Taylor LP (2014) found the classic criteria headache in this intracranial tumor is rare (Nelson & Taylor, 2014). Valentinis L. et al. (2010) found that only 5.1% of patients met the three "classic criteria"; thus, the ICHD criteria may have missed the criteria for headache due to brain tumors (Nelson & Taylor, 2014; Valentinis et al., 2009).

Patients with headaches are less likely to have intracranial tumors, whereas headaches are more common in patients with brain tumors. Only 2-8 % report having a headache as their sole symptom, according to clinical studies (Taylor, 2014). Patients with intracranial tumors may also have nausea and vomiting, seizures, loss of consciousness, and motor impairments in addition to headaches (Alentorn et al., 2016; Amidei & Kushner, 2015; Liigant et al., 2001; Pace et al., 2009).

The objectives of this paper was to investigate the prevalence of intracranial tumor headache as well as its clinical characteristics. Beside that, this paper also investigated into the prevalence of nausea/vomiting, seizures, loss of consciousness, and motor deficits.

2. RESEARCH METHOD

2.1. Research Design

This retrospective study was conducted using a cross-sectional design to determine the profile of headache and accompanying symptoms in patients with intracranial tumors for one year (January to December 2018) which was taken from the resume of inpatient medical records at the Department of Neurology, Dr. Hasan Sadikin Central General Hospital Bandung. All procedures carried out in this study were approved by the Medical Research Ethics Committee, Faculty of Medicine, University of Padjadjaran with serial number 730/UN6.KEP/EC/2020 and the Health Research Ethics Committee of Dr. Hasan Sadikin Central General Hospital Bandung with serial number LB.02.01/X.2.2.1/19930/2020.

2.2. Data Collection

Inclusion criteria in this study were all patient who diagnosed with intracranial tumors and hospitalized in the Department of Neurology, Dr. Hasan Sadikin Hospital Bandung, West Java, Indonesia. Neuroimaging through CT-Scan or clinical diagnosis based on clinical symptoms and the presence of tumors in other body areas were used to diagnose intracranial tumors in this study. The total population of cases of intracranial tumors that met the requirements for the research participants was used as the sample size in this study.

2.3. Statistic Analysis

The data is first entered into Excel and then analyzed using the *Statistical Package for the Social Science* (SPSS 26.0) software for Windows and is presented with percentages and appropriate tables.

3. RESULT AND DISCUSSION

3.1. Result Research

3.1.1. Research Population

This study used 93 medical record resumes, from the existing sample there were 44 (47,3%) males and 49 (52,7%) females. The mean age of the 93 subjects was 47,4 years and

PHARMACOLOGY, MEDICAL REPORTS, ORTHOPEDIC, AND ILLNESS DETAILS (COMORBID) Volume 1 ISSUE 1 (2022)

the median was 48 years. Of these subjects, 70 (86.4%) had headache, 11 (13.6%) had no headache, and 12 had no known headache status.

3.1.2. Basic characteristics of intracranial tumor study subjects

Based on the data, it was found that female (95.2%) were more likely to experience headaches than male (76.9%). The mean and median of subjects with headache were 46.6 years and 47 years, while the mean and median of subjects without headache were 53.2 years and 52 years, respectively. The tumor locations of the available 85 subject data were 77 (90.6%) supratentorial and 8 (9.4%) infratentorial. Subjects with supratentorial tumors were more likely to experience headaches (87.9%) than infratentorial tumors (71.4%).

In this study only 5 out of 70 (7.1%) subjects experienced headache as the only symptom. The majority of the subjects (60.2%) had decreased consciousness when they came to the neurology department. A total of 60 (64.5%) subjects had motor deficits. Nausea and vomiting occurred in 29 (31.9%) subjects, and no patient had nausea and vomiting without headache was found. The lowest prevalence of seizures compared to other concomitant symptoms in this study, only occurred in 22 (24.2%) subjects.

Table 1 Basic characteristics of intracranial tumor study subjects

| | With Headache | No Headache | Unknown | Amount | |
|---|------------------|----------------|--------------|--------------|--|
| | (Subject=70) | (Subject=11) | (Subject=12) | (Subject=93) | |
| Gender, subject (%) | | | | | |
| Male | 30(76,9) | 9(23,1) | 5 | 44(47,3) | |
| Female | 40(95,2) | 2(4,8) | 7 | 49(52,7) | |
| Age | | | | | |
| Mean, years | 46,6 | 53,2 | 46,5 | 47,4 | |
| Median, year | 47 | 52 | 49 | 48 | |
| Intracranial tumor location, subjects (%) | | | | | |
| Supertentorial | 58(87,9) | 8(12,1) | 11 | 77(90,6) | |
| Infratentorial | 5(71,4) | 2(28,6) | 1 | 8(9,4) | |
| Unknown | 7 | 1 | 0 | 8 | |
| Symptoms and signs, patient | | | | | |
| Decreased Consciousness, subject (%) | | | | | |
| Occur | 39(86,7) | 6(13,3) | 11 | 56(60,2) | |
| Not Occurred | 31(86,1) | 5(13,9) | 1 | 37(39,8) | |
| Motor Deficit, subject (%) | | | | | |
| Occur | 43(80,9) | 9(19,1) | 8 | 60(64,5) | |
| Not Occurred | 27(93,1) | 2(6,9) | 4 | 33(35,5) | |
| Nausea/Vomiting, subject (%) | | | | | |
| Occur | 27(100) | 0(0) | 2 | 29(31,9) | |
| Not Occurred | 42(79,2) | 11(20,8) | 9 | 62(68,1) | |
| Unknown | 1 | 0 | 1 | 2 | |

Seizures, subject (%)

| Occur | 13(72,2) | 5(27,8) | 4 | 22(24,2) |
|--------------|----------|---------|---|----------|
| Not Occurred | 56(90,3) | 6(9,7) | 7 | 69(75,8) |
| Unknown | 1 | 0 | 1 | 2 |

3.1.3. Headache Profile

The following is a headache profile in subjects based on intensity, location of pain, progression, and onset of headache. The known headache intensity in this study was 34 subjects, with a mean of 6,4; median 6,5; 10th percentile is 4,5; and the 90th percentile is 8,5. Headache occurred unilaterally in 12 (37.5%) subjects and bilaterally in 20 (62.5%) subjects, among 12 subjects who had unilateral headache, 7 (21.9%) had left-sided headache and 5 (15.6%) experienced right-sided headache. Headache progression occurred in 29 (93.5%) subjects and only 2 (6.5%) subjects did not experience progression.

Furthermore, headache onset before hospital admission in patients with intracranial tumors was as follows, <3 days occurred in 4 (7.7%) subjects, 3-30 days in 21 subjects (40.4%), >30 days -6 months occurred in 20 (38.5%) subjects, >6 months -1 year in 3 (5.7%) subjects, >1 year -2 years occurred in 3 (5.7%) subjects, >2 years -5 years occurred in 1 (1.9%) subject, and none had headache onset more than 5 years.

Table 2 Headache Profile based on Intensity, Location, Progressivity, and Onset.

| Headache Profile | Number | Percentage (%) |
|---------------------|--------|----------------|
| Intensity | | |
| 10th percentile | 4,5 | - |
| Median | 6,5 | - |
| 90th percentile | 8,5 | - |
| Average | 6,4 | - |
| Side Location | | |
| Left | 7 | 21,9 |
| Right | 5 | 15,6 |
| Bilateral | 20 | 62,5 |
| No Pain | 11 | - |
| Unknown | 50 | - |
| Progressivity | | |
| Occur | 29 | 93,5 |
| Not Occurred | 2 | 6,5 |
| No Pain | 11 | - |
| Unknown | 51 | - |
| Onset | | |
| <3 Days | 4 | 7.7 |
| 3-30 Days | 21 | 40.4 |
| >30 Days - 6 Months | 20 | 38.5 |
| >6 Months – 1 Year | 3 | 5.7 |
| >1 year - 2 Years | 3 | 5.7 |
| >2 years - 5 Years | 1 | 1.9 |

PHARMACOLOGY, MEDICAL REPORTS, ORTHOPEDIC, AND ILLNESS DETAILS (COMORBID) Volume 1 ISSUE 1 (2022)

| No Pain | 11 | - |
|---------|----|---|
| Unknown | 30 | - |

3.1.4. Relationship between Headache Location and Intracranial Tumor Location

Subjects who experienced bilateral headaches were 20 patients and then divided based on the location of the tumor: 6 bilateral, 5 right, 8 left, and 1 unknown. Subjects who experienced headaches on the right side as many as 5 patients and then divided based on the location of the tumor, 1 bilateral, 3 right, and 1 left. Subjects who experienced headaches on the left side as many as 7 subjects and then divided based on the location of the tumor, 1 bilateral, 1 right, 4 left, and 1 unknown.

| Table 3 Relationship between Tumor Location and Headache Locatio | n |
|--|---|
|--|---|

| | | Tumor Location | | | _ | | |
|----------------------|-----------|----------------|-------|------|---------|-------|--|
| | | Bilateral | Right | Left | Unknown | Total | |
| Headache Location | Bilateral | 6 | 5 | 8 | 1 | 20 | |
| | Right | 1 | 3 | 1 | 0 | 5 | |
| | Left | 1 | 1 | 4 | 1 | 7 | |
| | No Pain | 1 | 3 | 6 | 1 | 11 | |
| | Unknown | 11 | 18 | 16 | 5 | 50 | |
| | Total | 20 | 30 | 35 | 8 | 93 | |

4.2. Discussion

4.2.1. Relationship Between Headaches and Age

Intracranial tumor patients who experienced headache had a younger mean and median age than those without headache. Patients who experienced headache had a mean and median of 46,6 and 47 years, compared with those without headache 53,2 and 52 years, respectively. These data are in accordance with research conducted by L. Valentinis et al. (2009), Schankin CJ et al., and the reports of Lowry et al. that headaches are more common in younger patients. According to Lowry et al., this is associated with brain atrophy which causes the subarachnoid space and ventricles to become larger, hence allowing more expansion of the space occupying lesion (SOL) (Schankin et al., 2007; Valentinis et al., 2009).

4.2.2. Prevalence of Associated Symptoms

In this study only 5 of 69 (7.2%) subjects experienced headache as the only symptom, this result is in accordance with the literature review conducted by Taylor LP that only 2-8% of intracranial tumor patients experienced headache as a symptom. the only symptom (Taylor, 2014). In this study 60 (64.5%) patients had motor deficits. Reports of the incidence of motor deficits vary widely from 10-91%, one of the reasons for this difference is due to overlapping and inconsistency of terminology, for example ataxia and hemiparesis can cause gait disturbances (Amidei & Kushner, 2015).

In this study, there were 54 (59.3%) subjects who had decreased consciousness. According to the literature review conducted by Tobias Walbert and Muhib Khan (2014),

loss of consciousness is the most common symptom (1-90%) in the last weeks of intracranial tumor patients. Confusion and delirium often precede loss of consciousness before the patient dies.

In this study, there were 29 (31.9%) subjects who experienced nausea/vomiting and none experienced nausea/vomiting without headache. L. Valentinis et al. found that the incidence of nausea/vomiting occurred in 34.7% of intracranial tumors with headache, nausea and vomiting indicated an increase in intracranial pressure, without an increase in intracranial pressure, headaches due to intracranial tumors were milder and less frequently associated with nausea/vomiting. Approximately 86-95% who experience increased intracranial pressure experience headaches (Nelson & Taylor, 2014; Valentinis et al., 2009).

This study found 22 (23.7%) subjects had seizures. Meanwhile, another study analyzing 711 subjects with primary and secondary intracranial tumors found that 165 (23%) subjects had had at least one seizure prior to the diagnosis of an intracranial tumor (Liigant et al., 2001).

4.2.3. Headache Profile

The intensity of headache experienced by the subjects in this study had a mean of 6,4; median 6,5; 10th percentile 4,5; and the 90th percentile 8,5. These findings are not significantly different from those of other research that have examined the same topic, such as study conducted by CJ Schankin et al. (2007) who obtain the result; 10th percentile 3,0; median 6,0, and 90th percentile 8,3. Further, another study conducted in 2009 by L. Valentinis et al., got a mean of 6,1 and a median of 6 (Schankin et al., 2007; Valentinis et al., 2009).

In this study, 32 subjects (62.5%) had bilateral headaches and 12 (37.5%) had unilateral headaches. These findings are not significantly different from a prospective study conducted by L. Valentinis et al., 61.2% of subjects had bilateral headaches, 33.7% of subjects had unilateral headaches, and 5.1% of subjects had both (Valentinis et al., 2009). In contrast, research in 2007 conducted by CJ Schankin et al. got quite different results, the number of subjects who experienced bilateral and unilateral headaches was almost the same, namely bilateral 49% and unilateral 51% (Schankin et al., 2007).

The progression of headaches recorded in the medical record resume was 32 subjects, and 29 (93.5%) of them experienced progressivity and the remaining 3 (6.5%) did not experience any progression. The percentage of patients with progressive headache found in other studies varies widely, in Valentinis L. et al. only found 30.6% of subjects who experienced headache progression, while Pfund et al. found 79.1% of subjects experienced headache progression (Pfund et al., 1999; Valentinis et al., 2009).

In this study, the most frequent onset of headache was 3 days – 6 months after admitting the hospital as many as 41 (78.8%) subjects. Whereas, in N. Suwanwela et al. only found 50.8% of subjects experienced headache onset 3 days – 6 months. Furthermore, this study also only found 7.7% of subjects who experienced headache onset with <3 days and 13.5% of subjects who experienced headache onset >6 months compared to the above study whose headache onset with <3 days was much less, namely only 3. 3% and the onset of headache with >6 months was much more, namely 45,9% (Suwanwela et al., 1994).

4.2.4. Relationship Between Headache Location and Tumor Location

PHARMACOLOGY, MEDICAL REPORTS, ORTHOPEDIC, AND ILLNESS DETAILS (COMORBID) Volume 1 ISSUE 1 (2022)

Patients who experienced bilateral headaches were 20 patients, then divided by tumor location 6 (31.6%) patients had bilateral intracranial tumors, 13 (68.4%) patients had right or left unilateral intracranial tumors, and 1 patient had unknown side. Patients who experienced unilateral headache were 12 patients, 7 (63.6%) patients had unilateral intracranial tumor on the same side, 2 (18.2%) patients had unilateral intracranial tumors, and 1 patient had unknown. Therefore, these findings are not significantly different from CJ Schankin et al., who found that 61,5% of the subjects had unilateral headaches and had tumors on the same side (Schankin et al., 2007).

4. CONCLUSION

Headache is a common feature of intracranial tumors, and is usually accompanied by accompanying symptoms, particularly motor deficits, loss of consciousness, nausea/vomiting, and seizures. The mean and median headache intensity experienced by subjects with intracranial tumors on a scale of 1-10 were 6,4 and 6,5, respectively. Subjects were most likely to have bilateral headaches, and subjects who had unilateral headaches had a unilateral intracranial tumor on the same side of the headache. Almost all subjects experienced progressive headaches. The onset of headache in subjects before hospital admission was generally 3 days – 6 months.

REFERENCES

- Alentorn, A., Hoang-Xuan, K., & Mikkelsen, T. (2016). Presenting signs and symptoms in brain tumors. *Handbook of Clinical Neurology*, 134, 19–26.
- Amidei, C., & Kushner, D. S. (2015). Clinical implications of motor deficits related to brain tumors. *Neuro-Oncology Practice*, *2*(4), 179–184.
- Arnold, M. (2018). Headache classification committee of the international headache society (IHS) the international classification of headache disorders. *Cephalalgia*, 38(1), 1–211.
- Liigant, A., Haldre, S., Õun, A., Linnamägi, Ü., Saar, A., Asser, T., & Kaasik, A.-E. (2001). Seizure disorders in patients with brain tumors. *European Neurology*, 45(1), 46–51.
- Nelson, S., & Taylor, L. P. (2014). Headaches in brain tumor patients: primary or secondary? *Headache: The Journal of Head and Face Pain*, 54(4), 776–785.
- Pace, A., di Lorenzo, C., Guariglia, L., Jandolo, B., Carapella, C. M., & Pompili, A. (2009). End of life issues in brain tumor patients. *Journal of Neuro-Oncology*, 91(1), 39–43.
- Pfund, Z., Szapary, L., Jaszberenyi, O., Nagy, F., & Czopf, J. (1999). Headache in intracranial tumors. *Cephalalgia*, 19(9), 787–790.
- Schankin, C. J., Ferrari, U., Reinisch, V. M., Birnbaum, T., Goldbrunner, R., & Straube, A. (2007). Characteristics of brain tumour-associated headache. *Cephalalgia*, 27(8), 904–911.
- Suwanwela, N., Phanthumchinda, K., & Kaoropthum, S. (1994). Headache in brain tumor: a cross-sectional study. *Headache: The Journal of Head and Face Pain*, 34(7), 435–438.

- Taylor, L. P. (2014). Mechanism of brain tumor headache. *Headache: The Journal of Head and Face Pain*, 54(4), 772–775.
- Valentinis, L., Tuniz, F., Valent, F., Mucchiut, M., Little, D., Skrap, M., Bergonzi, P., & Zanchin, G. (2009). Headache attributed to intracranial tumours: a prospective cohort study. *Cephalalgia*, no-no.
- Walbert, T., & Khan, M. (2014). End-of-life symptoms and care in patients with primary malignant brain tumors: a systematic literature review. *Journal of Neuro-Oncology*, 117(2), 217–224.
- WHO. (2018). Headache Disorders. http://www.who.int/mediacentre/factsheets/fs277/en/